# Summary of Safety and Effectiveness Data (SSED)

## I. GENERAL INFORMATION

Device Generic Name: Iliac Stent

Device Trade Name: EverFlex™ Self- Expanding Peripheral Stent System

Device Product Code: NIO

Applicants Name and Address: ev3, Inc.
3033 Campus Drive, Suite, #N550
Plymouth, MN 55441

Dates of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P110023/S007

Date of FDA Notice of Approval: October 10, 2014

Priority Review: Not Applicable

The original PMA (P110023) was approved on March 7, 2012 and is indicated to improve luminal diameter in the treatment of stenotic, restenotic or occluded lesions up to 180 mm in length in the native superficial femoral artery or superficial femoral and proximal popliteal arteries with reference vessel diameter ranging from 4.5 – 7.5mm. The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the EverFlex™ Self- Expanding Peripheral Stent System to include use in common and/or external iliac arteries.

## II. INDICATION FOR USE

The EverFlex™ Self-expanding Peripheral Stent System is indicated for improving luminal diameter in patients with atherosclerotic disease of the common and/or external iliac arteries up to and including 100 mm in length, with a reference vessel diameter of 4.5 – 7.5 mm.

## III. CONTRAINDICATIONS

- Patients with known hypersensitivity to nickel-titanium
- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system.

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the EverFlex™ Self-Expanding Peripheral Stent System labeling (Instructions for Use).

## V. DEVICE DESCRIPTION

The EverFlex™ Self-Expanding Peripheral Stent System (EverFlex) consists of a self-expanding nitinol stent pre-mounted on an over-the-wire stent delivery system. **Table 1** lists the available stent diameters and lengths for the EverFlex™ Self-Expanding Peripheral Stent System for iliac indication.

**Table 1: EverFlex Stent Diameters and Lengths**

| | | Stent Length (mm) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | **20** | **30** | **40** | **60** | **80** | **100** | **120** |
| **Stent Diameter (mm)** | **6** | x | x | x | x | x | x | x |
| | **7** | x | x | x | x | x | x | x |
| | **8** | x | x | x | x | x | x | x |

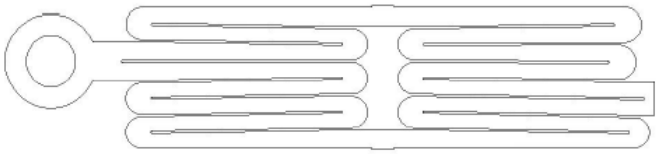

**Figure1**: Laser Cut Everflex Stent

The nitinol stent is laser machined from a continuous non-welded (seamless) piece of nitinol tubing into an open lattice design. The EverFlex stent cell geometry, shown in **Figure 1**, includes three (3) wave peaks between connection bridges and uses an alternating off-line pattern for the connection bridges which is intended to increase stent flexibility. Tantalum radiopaque markers are located on both ends of the stent to aid in visualization.

The stent is pre-mounted on an 80 or 120 cm working length 6F, .035" over-the-wire (OTW) stent delivery system that is comprised of multiple components as shown in **Figure 2**. Radiopaque markers on the stent delivery system are intended to aid in the accurate placement of the stent. Deployment is achieved by pulling the distal delivery system handle proximally, which retracts the outer sheath. The delivery system radiopaque stent retainer holds the stent stationary until the outer sheath is fully retracted to facilitate accurate placement. Upon deployment, the stent achieves its pre-determined diameter and exerts a constant, gentle outward force to maintain patency in the target vessel.

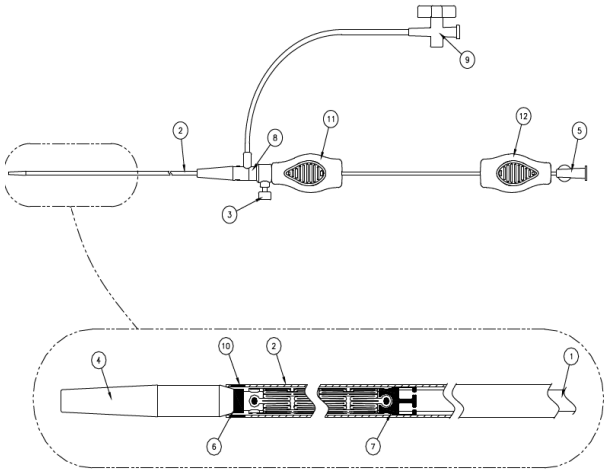

**Figure 2 – Delivery System**

1. Inner Subassembly
2. Outer Subassembly
3. Safety Lock
4. Distal Catheter Tip
5. Proximal Hub
6. Inner Subassembly Distal Marker Band
7. Inner Subassembly Proximal Marker Band/Retainer
8. Manifold Subassembly
9. Stopcock
10. Outer Subassembly Distal Marker Band
11. Distal Grip
12. Proximal Grip

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for treatment of atherosclerotic disease of the common and/or external iliac arteries with non-invasive lifestyle modifications including exercise, weight control, cessation of smoking and drug therapy; minimally invasive endovascular intervention with balloon angioplasty, stent placement using other FDA-approved peripheral stents. Each alternative has its own advantages and disadvantages. A patient should fully discuss those alternatives with his/her physician to select the method that best meets expectations and lifestyle.

## VII. MARKETING HISTORY

The Protégé® EverFlex™ Self-Expanding Peripheral Stent System has been commercially available in the European Union (EU) since March, 2006. The Protégé® EverFlex™ Self-Expanding Biliary Stent System has been commercially available in the United States since March, 2006, and the EverFlex™ Self-Expanding Peripheral Stent System has been commercially available in the United States since March, 2012 for the superficial femoral artery (SFA) and proximal popliteal artery (PPA) indication. The EverFlex™ Self-Expanding Peripheral Stent System presented in this PMA Supplement is identical to the Protégé® EverFlex™ Self-Expanding Peripheral Stent System commercially available in the EU and the EverFlex™ Self-Expanding Peripheral Stent System commercially available in the United States.

The Protégé® EverFlex™ Self-Expanding Stent System and the EverFlex™ Self-Expanding Peripheral Stent System have remained in continuous distribution since commercial introduction and have not been withdrawn from marketing in any country.

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects (e.g., complications) that may occur and/or require intervention with the use of this device include, but are not limited to:

- Abrupt or sub-acute closure
- Allergic reaction to device materials or procedure medications
- Allergic reaction to Nitinol
- Amputation
- Aneurysm
- Angina
- Arrhythmia
- Arterio-venous fistula
- Artery injury (e.g. dissection, perforation, or rupture)
- Bleeding requiring transfusion
- Bruising
- Contrast medium reaction/renal failure
- Death
- Device breakage
- Edema
- Embolism
- Failure to deploy stent
- Fever
- Gastrointestinal bleeding due to anticoagulation
- Hematoma
- Hypertension/Hypotension
- Infection
- Inflammation
- Intraluminal thrombus
- Myocardial Infarction
- Pain
- Partial stent deployment
- Pseudoaneurysm
- Renal failure
- Renal insufficiency
- Restenosis
- Sepsis
- Shock
- Stent collapse or fracture
- Stent migration
- Stent misplacement
- Stroke
- Surgical or endovascular intervention
- Thrombosis/occlusion of the stent
- Transient Ischemic Attack
- Venous Thromboembolism
- Vessel spasm
- Worsening claudication or rest pain

For the adverse events that occurred in the clinical study, please see

**Table** 7.

## IX. SUMMARY OF PRECLINICAL STUDIES

The pre-clinical tests listed below were leveraged from the original submission to support the iliac indication. The pre-clinical data reviewed under P110023 was found to be adequate to support the new indication of treatment in the common and/or external iliac arteries.

- Engineering
- Pre-clinical animal studies
- Biocompatibility
- Sterilization
- Packaging

- Shelf-life

## X. SUMMARY OF PRIMARY CLINICAL STUDY

### A. Confirmatory Clinical Study Design

The applicant previously conducted a study titled the US StuDy for EvalUating EndovasculaR TreAtments of Lesions in the Superficial Femoral Artery and Proximal Popliteal By usIng the EverfLex NitInol STent SYstem II (DURABILITY II) study. DURABILITY II provided data to support the safety and effectiveness of the EverFlex™ Self-Expanding Peripheral Stent System in the superficial femoral and proximal popliteal arteries.

The DURABILITY Iliac study was a prospective, multi-center, non-randomized, single arm study to evaluate the EverFlex™ Self-Expanding Peripheral Stent System and the Protégé™ GPS Self-Expanding Stent System for the treatment of stenotic, restenotic (from PTA or adjunct therapy, not including stents or stent grafts) or occluded lesions of the common and/or external iliac arteries.

The objective of the study was to confirm the safety and effectiveness of the primary stenting. A total of 75 subjects were enrolled at 13 US and two European investigational sites; 31 of the 75 subjects had an EverFlex stent implanted and the larger diameter GPS stent was implanted in the other 44 patients. Subject follow-up occurred at pre-discharge, 30 days, 9 months, 1, 2 and 3 years post-procedure. The primary outcome for the study was Major Adverse Event (MAE) rate at 9 months. Secondary outcomes were MAE rate at 30 days, primary patency rate at 9 months, change of ankle-brachial index (ABI) at 30 days and 9 months, device success, change in walking impairment questionnaire score at 30 days and 9 months, and clinically driven target vessel revascularization at 30 days and 9 months.

DURABILITY Iliac Clinical Inclusion and Exclusion Criteria

Subjects enrolled in the DURABILITY Iliac study were required to meet the following general and angiographic **inclusion** criteria. Potential study Subjects who meet any of the following general and angiographic **exclusion** criteria were not eligible for enrollment in the study. **Table 4** lists all of the Inclusion and Exclusion Criteria

**Table 2: Inclusion and Exclusion Criteria**

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| 1. Has a Rutherford Clinical Category Score of 2, 3 or 4 per clinical description.<br>2. Is willing to comply with all follow-up evaluations at the specified times.<br>3. Is ≥ 18 years old.<br>4. Provides written informed consent prior to any enrollment screening procedures.<br>5. Target lesion(s) located within the native common and/or external iliac artery: proximal point at or distal to the ostium of the common iliac artery and distal point at least 1 cm above the inguinal ligament measured by straight anteroposterior (AP) | 1. Previous implantation of stent(s) in the target vessel.<br>2. Has received endovascular treatment of the target lesion within six months prior to the index procedure.<br>3. Has a contraindication or known untreatable allergy to antiplatelet therapy, anticoagulants, thrombolytic drugs or any other drug used during the study according to the protocol.<br>4. Has known hypersensitivity to contrast material that cannot be adequately pretreated.<br>5. Has known hypersensitivity to nickel-titanium.<br>6. Has bleeding diathesis, coagulopathy, known |

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| view.<br>6. Evidence of ≥ 50% stenosis or restenosis (from PTA or adjunct therapy, not including stents or stent grafts), or occlusion of target lesion(s) in the common iliac artery and/or external iliac artery.<br>7. Length of lesion(s) is ≤ 10 cm as determined by a spatially calibrated internal measurement using a device with known distance between radiopaque markers (e.g. marker catheter, balloon catheter, marker wire) and is amenable to stenting.<br>8. Target vessel diameter is ≥ 4.5 mm and ≤ 11.0 mm.<br>9. Evidence of patent common femoral artery and origin of *profunda femoris.*<br>10. Evidence of at least one patent infrapopliteal artery of the target limb that does not require treatment for significant stenosis (> 50% stenosis or occlusion) during the index procedure. | hypercoagulable condition, or refuses blood transfusion.<br>7. Is female currently breastfeeding, pregnant, or of childbearing potential not using adequate contraceptives measures.<br>8. Has life expectancy of less than 1 year.<br>9. Has planned use of cutting balloon, scoring balloon, thrombectomy, atherectomy, brachytherapy, cryotherapy or laser devices to treat the common or external iliac arteries as well as the ipsilateral SFA/proximal popliteal during the index procedure.<br>10. Has any planned surgical intervention (requiring hospitalization) or endovascular procedure 14 days before or 30 days after the index procedure.<br>11. Current Participation in an investigational drug or other device study.<br>12. Previously enrolled in this study.<br>13. Has known aortic aneurysm(s) > 5 cm.<br>14. Has one of the following co-morbid conditions:<br>♦ History of severe liver disease (i.e. ascites, esophageal varices, liver transplant)<br>♦ Known or suspected active infection<br>♦ Undergoing hemodialysis for kidney failure<br>♦ Undergoing immunosuppressant therapy<br>♦ Elevated creatinine level on most recent test (> 2.5 mg/dl)<br>♦ New York Heart Association Classification of III or IV with hospitalization for decompensated heart failure within 3 months<br>♦ Recent (within 30 days) myocardial infarction<br>♦ Recent (within 30 days) hemorrhagic or ischemic stroke<br>♦ Acute thrombophlebitis or deep venous thrombosis in the limb to be treated<br>♦ Any other co-morbid condition that in the judgment of the physician precludes safe percutaneous intervention<br>15. Guidewire or investigational device catheter cannot cross the target lesion(s) and re-enter true vessel lumen beyond the lesion(s).<br>16. Aneurysmal target vessel.<br>17. Presence of an acute intraluminal thrombus of the proposed lesion site.<br>18. If treatment is required of a non-target lesion distal to the target vessel during the index procedure, the non-target lesion must be successfully treated (residual stenosis < 30%) prior to treatment of the target lesion and:<br>♦ Be located within the native SFA/proximal popliteal<br>♦ The distal point must be at least 3 cm above the cortical margin of the femur<br>♦ The proximal point must be at least 1 cm below |

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| | the origin of the *profunda femoris*<br>♦ Total lesion length is ≤ 10 cm<br>19. Lack of straight-line blood flow to the foot/ankle of the target limb prior to index procedure or inability to achieve straight-line blood flow to the foot/ankle of the target limb through treatment of a non-target lesion in the SFA/proximal popliteal during index procedure prior to enrollment.<br>20. Perforation, dissection or other injury requiring additional stenting or surgical intervention prior to the start of target lesion treatment. |

DURABILITY Iliac Study Conduct

All subjects were assessed at baseline prior to the study procedure, then again at pre-discharge, 30 days, 9 months, 1, 2 and 3 years post-procedure. **Table 3** provides a summary of the specific study assessment requirements and timeframes at each stage of the study.

**Table 3: Study Assessment Schedule and Requirements**

| Assessment Schedule (Timeframe Window) | Baseline (30 days prior, labs 7 days prior to enrollment) | Procedure | Pre-Discharge (within 7 days post-procedure) | 30 Days (25-40 Days post-procedure) | 9 Months (240-300 days post-procedure) | 1, 2 & 3 Years* |
|---|---|---|---|---|---|---|
| Informed Consent | X | | | | | |
| Medical history | X | | | | | |
| Physical exam | X | | | | | |
| Concomitant medication history | X | X | X | X | X | |
| Rutherford Clinical Category | X | | | X | X | |
| Ankle-brachial index | X | | | X | X | |
| Walking Impairment Questionnaire | X | | | X | X | |
| Duplex ultrasound | | | | | X | |
| Laboratory tests§ | X | | | | | |
| Angiogram | | X | | | | |
| Adverse event evaluation | | X | X | X | X | X |

*Annual visits could be conducted by telephone; 320-410 (1-Year), 685-775 (2-Year), and 1050-1140 (3-Year) days post-procedure.

§Creatinine and Complete Blood Count

DURABILITY Iliac Study Outcomes

The primary outcome for the DURABILITY Iliac study was the Major Adverse Event (MAE) rate at 9 months, defined as a composite of periprocedural death, in-hospital MI, clinically-driven target lesion revascularization (TLR) and amputation of the treated limb through 9 months post-procedure.

The secondary outcomes for the DURABILITY Iliac study included:

- Major Adverse Event rate at 30 days defined as a composite of periprocedural death, in-hospital MI, clinically-driven target lesion revascularization and amputation of the treated limb through 30 days post-procedure.
- Primary patency rate at 9 months defined as a binary duplex ultrasound ratio ≤ 2.4 at the stented target lesion with no clinically-driven re-intervention within the stented segment.
- Change of Ankle-Brachial Index (ABI) at 30 days and 9 months defined as a change of the ABI compared to baseline in subjects with compressible arteries and baseline ABI < 0.9 through 30 days and 9 months post-procedure.
- Device success, defined as the ability to deploy the stent as intended at the treatment site.
- Change in Walking Impairment Questionnaire (WIQ) score at 30 days and 9 months defined as change in WIQ score compared to baseline through 30 days and 9 months post-procedure.
- Clinically-driven Target Vessel Revascularization (TVR) at 30 days and 9 months defined as any re-intervention or artery bypass graft surgery involving the target vessel in which the subject has a ≥ 50% diameter stenosis (per angiographic core lab assessment) in the presence of recurrent symptoms, or a ≥ 70% stenosis without any symptoms.

## B. Accountability of PMA Cohort

A total of 75 subjects signed the informed consent and were enrolled in the DURABILITY Iliac study; 31 of the 75 subjects had an EverFlex stent implanted. All 31/31 (100%) completed the pre-discharge follow-up visit, 96.8% (30/31) completed the 30-day follow-up visit, and 90.3% (28/31) completed the 9-month follow-up visit.

## C. Study Population Demographics and Baseline Parameters

Baseline demographic and clinical characteristics for subjects implanted with an EverFlex stent in the DURABILITY Iliac study are summarized in **Table 4**.

**Table 4: Demographics and Baseline Clinical Characteristics**

| Subject Characteristics | N=31* |
|---|---|
| Age (yrs.), Mean± SD (N), [Median] (Min, Max) | 62.6 ± 8.7 (31)<br>[64.0] (49.0 , 80.0) |
| Male | 54.8% (17/31) |
| Race | |
| Caucasian | 93.5% (29/31) |
| African American | 3.2% (1/31) |
| Asian | 0.0% (0/31) |
| American Indian or Alaska Native | 0.0% (0/31) |
| Native Hawaiian or other Pacific Islander | 3.2% (1/31) |
| Other | 0.0% (0/31) |
| Ethnicity | |
| Hispanic | 0.0% (0/31) |
| Not Hispanic | 100.0% (31/31) |
| **Risk Factors and Medical History** | |
| Diabetes | 16.1% (5/31) |
| Type I | 0.0% (0/5) |
| Type II | 100.0% (5/5) |

| Subject Characteristics | N=31* |
|---|---|
| Hyperlipidemia | 58.1% (18/31) |
| Hypertension | 74.2% (23/31) |
| Renal insufficiency | 3.2% (1/31) |
| Current smoker | 61.3% (19/31) |
| Angina | 6.5% (2/31) |
| Arrhythmia | 6.5% (2/31) |
| Congestive Heart Failure (CHF) | 9.7% (3/31) |
| Stroke | 9.7% (3/31) |
| Transient Ischemic Attack (TIA) | 9.7% (3/31) |
| Myocardial Infarction (MI) | 6.5% (2/31) |
| No-healing ischemic ulcers in the lower extremities | 0.0% (0/31) |
| Amputation of the lower extremities | 0.0% (0/31) |
| Peripheral Intervention** | 19.4% (6/31) |
| **Clinical Characteristics** | |
| Rutherford Clinical Category | |
| 2=Moderate claudication | 45.2% (14/31) |
| 3=Severe claudication | 51.6% (16/31) |
| 4=Ischemic rest pain | 3.2% (1/31) |
| Ankle-Brachial Index (ABI) | 0.68 ± 0.15 (30)<br>[0.69] (0.29 , 0.95) |

*A total of 31/75 subjects were implanted with the EverFlex stent in the DURABILITY Iliac study.

**Types of historical peripheral interventions included: PTA, Stenting, Atherectomy, or Bypass. There was no history of Cryoplasty, Laser or other types of interventions.

**Table 5** presents baseline target lesion characteristics assessed by the angiographic core laboratory for the lesions treated with the EverFlex stent. The mean pre-procedure percent diameter stenosis was 71.4%, including 18.8% occluded lesions and 25.0% severely calcified lesions.

**Table 5: Baseline Target Lesion Characteristics**

| Lesion Characteristics | N=32 (# of lesions)* |
|---|---|
| Right Iliac Artery | 56.3% (18/32) |
| Common | 44.4% (8/18) |
| External | 55.6% (10/18) |
| Left Iliac Artery | 43.8% (14/32) |
| Common | 71.4% (10/14) |
| External | 28.6% (4/14) |
| **Lesion Morphology** | |
| Distance from Ostium (mm) | 38.6 ± 38.4 (32)<br>[32.0] (0.0 , 129.4) |
| Lesion Length (mm) | 42.8 ± 25.8 (32)<br>[37.7] (7.0 , 114.9) |
| Eccentric Lesion | 53.1% (17/32) |
| Bend | 11.3 ± 7.0 (32)<br>[10.0] (0.0 , 30.0) |
| Thrombus | 0.0% (0/32) |
| Any Calcification | 56.3% (18/32) |
| None/Mild | 43.8% (14/32) |
| Moderate | 31.3% (10/32) |
| Severe | 25.0% (8/32) |

| Lesion Characteristics | N=32 (# of lesions)* |
|---|---|
| Ulceration present | 25.0% (8/32) |
| Aneurysm present | 9.4% (3/32) |
| **TASC II** | |
| Type A | 46.9% (15/32) |
| Type B | 40.6% (13/32) |
| Type C | 6.3% (2/32) |
| Type D | 6.3% (2/32) |
| **Quantitative Angiographic Results** | |
| Pre-procedure Reference Diameter (mm) | 6.7 ± 1.2 (32)<br>[6.8] (4.4 , 9.6) |
| Pre-procedure Minimal Lumen Diameter (mm) | 1.9 ± 1.2 (32)<br>[2.2] (0.0 , 4.2) |
| Pre-procedure % Diameter Stenosis | 71.4 ± 16.9 (32)<br>[69.5] (45.1 , 100.0) |
| Percent Total Occlusions (100% stenosis) | 18.8% (6/32) |

*A total of 32/77 lesions were treated with the EverFlex stent in the DURABILITY Iliac study.

## D. Confirmatory Safety and Effectiveness Results

Primary Outcome

The primary outcome of the study is MAE rate at 9 months (270 days) post-procedure. An MAE was defined as a composite of periprocedural death, in hospital MI, clinically-driven target lesion revascularization, and amputation of treated limb, as adjudicated by the Clinical Event Committee (CEC). The 9-month MAE rate for subjects implanted with the EverFlex stent was 0.0% (0/31). The Primary Outcome is presented in **Table 6**.

**Table 6: Summary of Primary Outcome**

| 9-Month MAE | N=31<br>%(n/N) [Events] |
|---|---|
| 9-Month MAE | 0.0%(0/31)[0] |
| Periprocedural Death | 0.0%(0/31)[0] |
| In-hospital MI | 0.0%(0/31)[0] |
| Clinically-driven TLR | 0.0%(0/31)[0] |
| Amputation of the Treated limb | 0.0%(0/31)[0] |

*A total of 31/75 subjects were implanted with the EverFlex stent in the DURABILITY Iliac study.

DURABILITY Iliac Adverse Events

**Table** 7 provides a summary of the CEC adjudicated serious adverse events (SAEs) for all subjects implanted with the EverFlex stent in the DURABILITY Iliac study. They are summarized by MedDRA System/Organ Class and include all reported serious adverse events, regardless of study device, study procedure or study requirement relatedness. The data are presented as a percentage of subjects experiencing AEs followed by the total number of events in brackets.

**Table 7: Summary of Serious Adverse Events**

| MedDRA System Organ Class (MedDRA Preferred Term) | ≤ 30 Days % (n/N) [Events] | ≤ 9 Months % (n/N) [Events] | ≤ 3 Years % (n/N) [Events] |
|---|---|---|---|
| **Total*** | **16.1% (5/31) [6]** | **41.9% (13/31) [24]** | **54.8% (17/31) [46]** |
| **Cardiac disorders** (Angina unstable, Cardiac failure congestive) | 0.0% (0/31) [0] | 9.7% (3/31) [5] | 9.7% (3/31) [7] |
| **Gastrointestinal disorders** (Anal fistula) | 0.0% (0/31) [0] | 0.0% (0/31) [0] | 3.2% (1/31) [1] |
| **Infections and infestations** (Pneumonia, Urinary tract infection) | 3.2% (1/31) [1] | 3.2% (1/31) [1] | 6.5% (2/31) [2] |
| **Injury, poisoning and procedural complications** (Arterial injury, In-stent arterial restenosis) | 0.0% (0/31) [0] | 6.5% (2/31) [2] | 12.9% (4/31) [5] |
| **Neoplasms benign, malignant and unspecified (incl cysts and polyps)** (Basal cell carcinoma, Lung neoplasm malignant, Non-Hodgkin's lymphoma recurrent, Pancreatic carcinoma, Skin cancer) | 6.5% (2/31) [2] | 9.7% (3/31) [3] | 16.1% (5/31) [5] |
| **Nervous system disorders** (Carpal tunnel syndrome, Cerebrovascular accident, Transient ischaemic attack) | 0.0% (0/31) [0] | 6.5% (2/31) [2] | 9.7% (3/31) [3] |
| **Reproductive system and breast disorders** (Breast mass) | 0.0% (0/31) [0] | 0.0% (0/31) [0] | 3.2% (1/31) [1] |
| **Respiratory, thoracic and mediastinal disorders**** (Chronic obstructive pulmonary disease, Respiratory distress) | 0.0% (0/31) [0] | 0.0% (0/31) [0] | 6.5% (2/31) [2] |
| **Vascular disorders** (Arterial stenosis, Artery dissection, Artery occlusion, Hypotension, Iliac artery stenosis, Peripheral artery dissection) | 6.5% (2/31) [3] | 16.1% (5/31) [11] | 29.0% (9/31) [20] |

*A total of 31/75 subjects were implanted with the EverFlex stent in the DURABILITY Iliac study.

**There was one (1) death that occurred in the study. The event that caused the death was categorized under "Respiratory, thoracic and mediastinal disorder". The event that caused the death was adjudicated by the CEC as not related to the device, procedure or study requirements.

Outcome Summary

**Table 8** provides a summary of the primary and secondary Outcome measures for the 31 subjects implanted with the EverFlex stent in the DURABILITY Iliac study.

**Table 8: Summary of Primary and Secondary Outcomes**

| **Primary Outcome Measures** | **N=31*** |
|---|---|
| 9-Month MAE[1] | 0.0%(0/31)[0] |
| Periprocedural Death | 0.0%(0/31)[0] |
| In-hospital MI | 0.0%(0/31)[0] |
| Clinically-driven TLR | 0.0%(0/31)[0] |
| Amputation of the Treated limb | 0.0%(0/31)[0] |
| Freedom from 9-Month MAE -KM Estimate | 100.0% |

| Secondary Outcome Measures | N=31* |
|---|---|
| 30-Day MAE[1] | 0.0%(0/31)[0] |
| Periprocedural Death | 0.0%(0/31)[0] |
| In-hospital MI | 0.0%(0/31)[0] |
| Clinically driven TLR | 0.0%(0/31)[0] |
| Amputation of the Treated limb | 0.0%(0/31)[0] |
| Primary Patency Rate at 9 Months - KM Estimate[2] | 93.2% |
| Device Success[3] | 100.0% (32/32)* |
| Freedom from clinically-driven TVR at 30 days -KM Estimate | 100.0% |
| Freedom from clinically-driven TVR at 9 months KM Estimate | 100.0% |

*A total of 31/75 subjects were implanted with the EverFlex stent in the DURABILITY Iliac study.

* A total of 31 subjects with 32 target lesions were implanted with the EverFlex stent. One subject had two target lesions, one treated with the Protégé GPS stent and one treated with the EverFlex stent

1 Numbers are % (n/N) [Events]

2 Primary patency rate defined as a binary duplex ultrasound ratio ≤ 2.4 at the stented target lesion with no clinically-driven re-intervention within the stented segment

3 Device success was defined as the ability to deploy the stent as intended at the treatment site. The denominator includes number of stent implanted

## E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to any clinical investigator, financial interests, and arrangement of any clinical investigator conducting clinical studies covered by the regulation. The confirmatory clinical study included fifty five (55) investigators of which none were full-time or part-time employees of the sponsor and two (2) of the 55 investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: two (2) investigators
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

## XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

No supplemental clinical data was available or needed.

## XII. PANEL MEETING RECOMMENDATION

In accordance with the provisions of Section 515 (c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

## XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Safety and Effective Conclusions

The applicant conducted a previous study titled the US StuDy for EvalUating EndovasculaR TreAtments of Lesions in the Superficial Femoral Artery and Proximal Popliteal By usIng the EverfLex NitInol STent SYstem II (DURABILITY II) study. DURABILITY II provided data to support the safety and effectiveness of the EverFlex Self-Expanding Peripheral Stent System in the superficial femoral and proximal popliteal arteries.

Unlike stenting in vessels such as coronary, renal and iliac arteries, long-term patency following stenting in the superficial femoral artery (SFA) has been difficult to achieve.[1] Anatomically, when compared to the iliac arteries, the SFA is unique in that it is subject to movement in multiple planes during limb motion. Not only are there significant longitudinal vessel compression and elongation, but also radial compression, torsion, and flexion in response to musculoskeletal movement. Given the proven safety and effectiveness of the EverFlex™ Self-Expanding Peripheral Stent System in the superficial femoral and proximal popliteal arteries with the DURABILITY II study, the DURABILITY Iliac study was successfully completed to confirm safety and effectiveness of the EverFlex™ Self-Expanding Peripheral Stent System in the iliac arteries. Primary patency was 93.2% at 9 months and no MAE were reported. The mean ABI improved at 9 months and the WIQ also showed improvement in walking performance at 9 months. The DURABILITY Iliac multicenter confirmatory clinical study results demonstrates that the EverFlex™ Self-Expanding Peripheral Stent System is safe and effective for the treatment of atherosclerotic disease of the common and/or external iliac arteries.

### B. Benefit Risk Conclusions

Results of the pre-clinical studies were appropriately leveraged from the original PMA to support the safety and performance of the device in the iliac environment considering the SFA represents a more challenging anatomy than iliac arteries.[1] Patient follow-up from both the pivotal (P110023) and confirmatory clinical study (P110023/S007) was satisfactory with limited missing data. The probable benefit of the Everflex™ Self-expanding Peripheral Stent System in the ability to improve luminal diameter outweighs the probable risks associated with use of the device. Additional factors to be considered in determining probable risks and benefit for the EverFlex™ Self-Expanding Peripheral Stent System include:

- Patient follow-up was satisfactory. The serious adverse event (SAEs) was limited and the events were comparable to SAEs of similar devices.

- Most patients with the disease have symptoms only, but some patients may have tissue or limb loss. The disease is chronic and affects the mobility of the patient and the quality of life. It is treatable but not curable.

- There are alternative treatments available, but this treatment is perceived as less invasive than open surgery and more effective than percutaneous transluminal angioplasty. This treatment is highly valued by patients and preferred to the alternatives because it improves their quality of life without the need for open surgery.

In conclusion, given the available information obtained from both the DURABILITY II SFA pivotal study and the DURABILITY Iliac confirmatory study, the data suggests that the probable benefits of the Everflex™ Self-expanding Peripheral Stent System for the indicated use outweighs the probable risks.

### C. Overall Conclusions

The results from the confirmatory study provide reasonable assurance that the device is safe and effective therefore; it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

## XIV. CDRH DECISION

CDRH issued an approval order on October 10, 2014.

## XV. APPROVAL SPECIFICATION

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

## XVI. REFERENCES

1. Weinstock BS. Covered Stents in the Treatment of Superficial Femoral Artery Disease. Vascular Disease Management. 2014;11(4):76-86